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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/644,244	08/20/2003	Gustave Bergnes	7146P1	6081

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EXAMINER	
TRUONG, TAMTHOM NGO	
ART UNIT	**PAPER NUMBER**
1624	

DATE MAILED: 12/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/644,244	BERGNES, GUSTAVE	
	Examiner	Art Unit	
	Tamthom N. Truong	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *9-22-05 (Election)*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 21-37* is/are pending in the application.

4a) Of the above claim(s) *1,22-26 and 28-32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21,27 and 33-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/27 + 9/22/05*.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *attached* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

It is acknowledged that applicant has elected with traverse the invention of Group 14 (claims 21-23, 26-28 and 31-37 (in part)) in the reply of 9-22-05. Then, as per examiner's request, on 10-7-05, applicant has elected the following species on page 41:

- *3-benzyl-2-(1-bromo-2-methyl-propyl)-7-chloro-3H-pyrimido[4,5-d]pyrimidin-4-one;*
- *3-benzyl-2-(1-bromo-2-methyl-propyl)-6,7-dihydro-3H-thieno[3,2-d]pyrimidin-4-one.*

In view of the above elected species, Group 14 is further restricted as below:

Group 14a: Claims 21, 27 and 33-37 (in part), drawn to compounds of formula II with the following substituents:

T is CH_2, and U is also CH_2;

W is absent, C, or CH;

X is N or S;

Z is N, C or CH;

Pharmaceutical composition thereof and a method of treating cellular proliferative disease using said compounds; classified in class 514, subclasses 260.1, and 264.1; also class 544, subclasses 278 and 279.

Group 14b: Claims 1, 21-26, and 28-37 (in part), drawn to the remaining compounds of formula II, pharmaceutical composition thereof, and a method of treating cellular proliferative disease using said compounds; classified in classes 514 and 544, various

subclasses depending on the combination of W, X, Y and Z. Further restriction and/or election of species will be required.

Claims 1, 22-26 and 28-32 are withdrawn from consideration as being drawn to the non-elected subject matter.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. **Scope of Enablement:** Claims 34-37 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment (and not prevention) of cancers, does not reasonably provide enablement for the treatment or prevention of other diseases related to cellular proliferation such as: autoimmune disease, arthritis, graft rejection, inflammatory bowel disease, etc. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The following factors have been considered in the determination of an enabling disclosure:

(1) The breadth of the claims;

(2) The amount of direction or guidance presented;

(3) The state of the prior art;

(4) The relative skill of those in the art;

(5) The predictability or unpredictability of the art;

(6) The quantity of experimentation necessary;

[See ***Ex parte Forman***, 230 USPQ 546 (Bd. Pat. App. & Int., 1986); also ***In re Wands***, 858 F. 2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)].

The breadth of the claims:

Claim 34 recites: "*A method of treatment comprising administering an effective amount...to a patient suffering from a cellular proliferative disease.*"

Claim 35 depends on claim 34, but recites specific diseases of cellular proliferation.

Claim 36 recites: "*A method of treatment for a cellular proliferative disease...*"

Claim 37 recites: "*A kit comprising a compound...for treating a cellular proliferative disease...*"

By "treatment", the specification includes the following modalities:

[0076] a) preventing the disease, that is, causing the clinical symptoms of the disease not to develop;

[0077] b) inhibiting the disease, that is, slowing or arresting the development of clinical symptoms; and/or

[0078] c) relieving the disease, that is, causing the regression of clinical symptoms.

Thus, the scope of "treatment" alone is unduly broad. Likewise, the limitation of "cellular proliferative disease" covers cancer, hyperplasia, restenosis, cardiac hypertrophy, immune disorder or inflammation, etc. See the excerpt from pages 13-14 of the Pregrant Publication US 2004-0048853 A1.

Even for cancer alone, the scope of claims 34-37 covers many cancers that are very difficult (if not impossible) to treat such as: cardiac sarcoma, pancreas cancer, hepatoma, various cancers of the nervous system, neuroblastoma, etc. Because the limitation of "cellular proliferative disease" covers much more than just cancer, the scope of claims 34-37 is unduly broad.

The amount of direction or guidance presented:

The specification only outlines *in-vitro* bioassay procedures in Examples 7, 8 and 9. However, it is not clear which compounds have been tested, and what the IC_{50} values are for the tested compounds. Given the broad scope of compounds, and diseases to be treated, the description of *in-vitro* bioassay does not sufficiently guide a skilled clinician to effectively select a specific compound for a particular treatment. Thus, the specification fails to provide sufficient enablement for the intended scope of claims 34-37.

The state of the prior art:

Currently, in the practice of medicine, many chemotherapeutic agents (e.g., cisplastin, vincritine, vinblastine, doxorubicin, etc.) are not used to treat other diseases such as: arthritis, cardiac hypertrophy, immune disorder, or inflammation, etc. This is because chemotherapeutic agents are cytotoxic, and have a high risk:benefit ratio. Furthermore, as evident by the teaching

of **Mentrup et. al.** (US 3,846,549), a compound of heterocycle substituted piperazine has CNS depressant and antihypercholesteremic activities. Likewise, the teachings of **Press et. al.** (US 4,670,560), and **Cao et. al.** (US 2003/0096813 A1) relate compounds of thieno[3,2-d]pyrimidine with vasodilating or antidiabetic activities. Thus, the state of the art does not support the method of treatment as recited in the instant claims 34-37.

The relative skill of those in the art:

Even with the advanced training of M.D or Ph.D program, the skilled clinician would have to carry out more than routine experiment to select an effective compound from the genus of formula II, and use it in the treatment of various diseases. The skilled clinician would have to establish an LD_{50}, therapeutic index, and a pharmacokinetic profile for each compound in order to apply it in appropriate treatment. Such as task requires a lot of time, effort, and resources.

The predictability or unpredictability of the art, and **The quantity of experimentation necessary:**

The pharmaceutical art is known for its unpredictable. Likewise, the treatment of cancer alone has always been challenging since it is not easy to determine an effective dosage. Thus, given the broad scope of the claims, and the limited guidance, the skilled clinician would have to carry out undue experimentation to use the claimed compounds in a method of treatment recited in claims 34-37.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 21, 27 and 33-37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

a. Claim 21 recites many moieties with the phrase "*optionally substituted*". Said phrase renders the scope of all variables indefinite metes and bounds. In the absence of the specific moieties intended to effectuate modification by "substitution" or attachment to the chemical core claimed, the phrase "optionally substituted" renders the claim(s) in which it appears indefinite in all occurrences wherein applicant fails to articulate by chemical name, structural formula or sufficiently distinct functional language, the particular moieties applicant regards as those which will facilitate substitution, requisite to identifying the composition of matter claimed.

b. Claims 27 and 33-37 are rejected as being dependent on claim 21, and carrying over the indefinite limitations.

No pending claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tamthom N. Truong whose telephone number is 571-272-0676. The examiner can normally be reached on M-F (9:30-6:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Tamthom N. Truong
Examiner
Art Unit 1624

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11-04-05

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